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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/248,756	02/12/1999	LAURIE H GLIMCHER	HUI-021CN	9168
959	7590	12/16/2003	EXAMINER	
LAHIVE & COCKFIELD, LLP. 28 STATE STREET BOSTON, MA 02109			LEFFERS JR, GERALD G	
			ART UNIT	PAPER NUMBER

1636

DATE MAILED: 12/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

### Application No.

09/248,756

### Applicant(s)

GLIMMCHER, ET AL.

### Examiner

Gerald G Leffers Jr., PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11 September 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 35,36,38-40,42-49 and 56-67 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 35,36,38-40,42-49 and 56-67 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

Receipt is acknowledged of an amendment, filed 9/11/2003, in which claims were amended (claims 35 and 40) and in which new claims were presented (claims 57-67). Claims 35-36, 38-40, 42-49, 56-67 are pending in the instant application.

#### ***Response to Amendment***

The grounds of rejection of claims under 35 U.S.C. 112 2<sup>nd</sup> paragraph regarding the metes and bounds of the term "Maf family protein" have been withdrawn in view of the amendment to the claims, applicants' arguments and the state of the art. For example, Motohashi et al (Nucleic Acids Research, 1997, Vol. 25, No. 15, pages 2953-2959) make clear that at the time of the invention a large number of maf family proteins were known in the art as well as their cognate DNA sequences bound by the proteins.

The new grounds of rejection made herein were necessitated by applicants' amendment of the claims in the response filed 9/11/2003. This action is FINAL.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-36, 38-40, 42-49, 56-67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

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in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **These new grounds of rejection were necessitated by applicants' amendment of claim 35 in the amendment filed 9/11/03.**

Each of the rejected claims comprises the limitation "a maf family protein which binds to a MARE regulatory element of a Th2 associated cytokine gene and (ii) a target DNA comprising a MARE regulatory sequence of a Th2-associated cytokine gene". The response filed 9/11/03 points to specific passages in the specification for support (i.e. page 5, lines 20-24; page 8, lines 9-11). These passages are specific for c-maf binding of a MARE sequence linked to the IL-4 gene and merely provide support for c-maf binding to the MARE sequence associated with the IL-4 gene. The cited passages do not provide support for the concept of a broad range of maf family proteins that bind to a MARE sequence obtained from a Th2-associated gene. Therefore, the cited limitation is impermissible NEW MATTER.

In addition, the rejected claims encompass embodiments wherein the maf family protein must possess the ability to bind to a MARE sequence of a Th2-associated cytokine gene. The only Th2-associated cytokine shown in the prior art of record or the instant specification to possess a MARE sequence is the IL-4 gene and the only maf family protein shown to bind this particular MARE sequence is c-maf. The prior art and specification do not provide a structural/functional basis for the skilled artisan to envision those embodiments wherein a *different* Th2-associated cytokine gene comprises a MARE sequence is bound by a maf family protein. With the exception of v-maf, the prior art and specification do not provide a structural/functional basis for one of skill in the art to envision those embodiments where a *different* maf family protein binds the MARE sequence operatively linked to the IL-4 gene.

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Given the great similarity in structural/functional characteristics of c-maf and v-maf, the skilled artisan might reasonably expect that v-maf would bind the MARE sequence operatively linked to the IL-4 gene (e.g. Kataoka et al. Journal of Virology, 1993, Vol. 67, No. 4, pages 2133-2141).

Given that the rejected claims encompass a broad genus of *combinations* of maf family protein and MARE sequence of a Th2-associated cytokine gene, and given that only a single such combination has been described by the instant specification and prior art, the skilled artisan would not have been able to envision additional embodiments of the claimed invention.

Therefore, the skilled artisan would reasonably have concluded applicants were not in possession of the claimed invention.

Claims 35-36, 38-40, 42-49, 56-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for embodiments wherein the MARE sequence is the MARE regulatory sequence of the interleukin-4 gene and wherein the maf family protein is c-Maf, does not reasonably provide enablement for practicing the claimed invention with any other combination of MARE element and maf family protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. **These new grounds of rejection were necessitated by applicants' amendment of claim 35 in the amendment filed 9/11/03.**

The invention is complex, involving the specific interaction of a transcriptional regulatory protein with its cognate DNA sequence such that one can reasonably expect that a compound shown to modulate this interaction will be likely to affect the production of a Th2-

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associated cytokine. The crux of the invention is that the MARE element be one found within a Th2-associated cytokine gene and that the MARE element is one specifically bound by a maf family protein. The instant specification teaches that c-maf binds to a MARE element found within the gene for IL-4, a Th2-associated cytokine. No other combination of maf family protein and MARE element from a Th2-associated cytokine is taught by the specification or prior art. The prior art of record and the instant specification do not disclose any MARE element associated with any Th2-associated cytokine gene. In order to practice the claimed invention, the skilled artisan would have to first determine the presence of a MARE element that may be in functional proximity to an Th2-associated cytokine gene other than the IL-4 gene. The skilled artisan would then have to determine which maf family protein binds the MARE element and, importantly, if such binding leads to any modulation in production of the Th2-associated cytokine. All of which experimentation would be of an unpredictable, trial-and-error nature. Such experimentation must necessarily be considered as inventive over what is taught in the instant specification as there is no significant guidance to point towards any other specific combination of MARE element, Th2-associated gene and maf family protein. For these reasons, the instant application is not considered enabling for the broadly claimed invention.

### ***Response to Arguments/112 1<sup>st</sup> Rejections***

Applicant's arguments filed 9/11/03 in response to similar grounds of rejection of record have been considered, but are deemed as not persuasive. The response essentially argues several points: 1) enablement is not precluded by the necessity of some experimentation, 2) the amendment of the claims limits the scope to a maf family protein that binds to a MARE

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sequence of a Th2 associated cytokine gene and its cognate MARE sequence, **3)** the skilled artisan could readily identify such maf family proteins that bind the recited elements, **4)** c-maf has been shown to modulate IL-10 transcription as well as IL-4 production (e.g. Cao et al, Journal of Immunology, 2002, Vol. 169, pages 5715-5725), **5)** given the role of IL-4 in promoting Th2-associated cytokine production (e.g. IL-10), the effect of a compound on cytokine production could be measured by measuring these other, dependent cytokines, **6)** the examiner appears to doubt the utility for the claimed methods, and **7)** the specification has described a genus of maf family proteins and MARE responsive elements (e.g. structural information regarding the maf family of proteins and their cognate MARE responsive elements was known in the art).

At no point in making the rejections of record under 35 U.S.C. 112 has the examiner asserted or implied that the asserted utility of the claimed methods is not credible. The rejections have been made strictly under the requirements of 35 U.S.C. 112 1<sup>st</sup> paragraph. With regard to the amount of experimentation required in order for an invention to be enabled, the rejections made of record and made herein comprise a reasoned analysis of the different Wands factors. The lack of any significant teachings in the prior art and specification regarding the *combination* of a MARE response sequence of a Th2-associated cytokine and a cognate maf family protein makes practicing the claimed invention unpredictable and undue based upon the complexity of the invention and the work required. The examiner does not simply assert that the claimed invention is not enabled because some experimentation is required.

With regard to the description of the different maf family proteins and their cognate MARE sequences, the specification does teach that multiple maf family proteins were known in

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the art at the time of filing, as well as the presence of MARE sequences that the proteins bind. There is no description, however, in the specification and prior art of MARE sequences of Th2-associated cytokine genes bound by maf family proteins other than c-maf and the IL-4 MARE sequence. Therefore, there is no basis for the skilled artisan to envision the combination of elements critical to practicing the claimed invention.

*Examiner's Note*

Embodiments of the claimed methods limited to a combination of c-maf or v-maf and the MARE sequence element associated with the Th2-associated cytokine IL-4 would be allowable.

*Conclusion*

**No claims are allowed.**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,



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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr., PhD  
Primary Examiner  
Art Unit 1636

Ggl

  
**GERRY LEFFERS**  
**PRIMARY EXAMINER**